

**REMARKS**

The Office Action has been carefully reviewed. No claim is allowed. Claims 5, 9, 11, 12, 15-17 and 19 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 5, 9, 11, 12, 15-17 and 19 have been rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. This rejection is respectfully traversed.

The base claim (independent claim 9) is directed to a method for inhibiting angiogenesis in adipose tissue in mammals by administering leptin. The effect of leptin as an inhibitor of angiogenesis in adipose tissue of *ob*<sup>-/-</sup> mice, by inducing Ang-2 expression, is accepted by the examiner. However, the examiner challenges the extension of this effect to the adipose tissue of normal mammals, even though the examiner has no technical evidence to the contrary.

The examiner's attention is respectfully invited to Figure 7 and Example 7 (pages 27-28 of the present specification), which clearly show that the adipocytes of normal mice contain very low levels of VEGF. This is still the case even after administration of leptin, which strongly induces the expression of Ang-2. The up-regulation of Ang-2 was also demonstrated in adipose tissues of normal mice (Figure 4; see lanes 2 and 3). As it is known that, in the absence of VEGF, Ang-2 is angiostatic, one of skill in the art would have no reason to doubt, in view of the teaching and evidence provided in the present

application, that leptin is also angiostatic in the adipose tissues of normal mice, which contain very low levels of VEGF. Thus, the present specification does indeed provide guidance and examples in support of leptin inhibiting angiogenesis in adipose tissue of normal mice by inducing the expression of Ang-2.

Therefore, the present claims, which are drawn to a method of inhibiting angiogenesis by administering leptin, are enabled by the specification for both *ob*-/- mammals and normal mammals.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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